ASTORIA•PACIFIC

Neonatal Total Galactose Microplate Reagent Kit 510(k) Summary k121101

1. Name, Address of Contact Person

Applicant's name and address

JUN 20 2013

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Charles A. Peterson
President

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2. Name of the Device

Product Classification

Regulation Number	21 CFR 862.1310
510(k) Number	
Classification Panel	Clinical Chemistry
Product Code	JIA
Device Classification	Class I

Product Nomenclature

Common Name	Enzymatic Methods, Galactose
Classification Name	Galactose test system
Proprietary Name	Astoria-Pacific SPOTCHECK® Neonatal Total Galactose Microplate Reagent Kit

3. Identification of the legally-marketed device for which substantial equivalence is claimed.

Product Classification

Regulation Number	21 CFR 862.1310
510(k) Number	K991498
Classification Panel	Clinical Chemistry
Product Code	JIA
Device Classification	Class I

Product Nomenclature

Common Name	Enzymatic Methods, Galactose
Classification Name	Galactose test system
Proprietary Name	Accuwell Total Galactose
Model Number(s)	Accuwell Part No. 6020-20 EGAL, 2000 Test Kit

4. Description of the Device

SPOTCHECK Neonatal Total Galactose Microplate Reagent Kit

Astoria-Pacific 60 Plate Kit Part No. 81-2000-60K
Astoria-Pacific 5 Plate Kit Part No. 81-2000-05K
Galactose test system

KIT CONTENTS:

Extraction Solution
Enzyme Reagent
Coenzyme Reagent
Color Reagent
Stock Standard

Total Galactose is measured colorimetrically following the completion of two enzyme assisted reactions and the color formation reaction; details and descriptions are provided below:

The first reaction entails conversion of Galactose-1-Phosphate (Gal-1-P) to Galactose (Gal), catalyzed by alkaline phosphatase.

$$\text{Gal-1-P} \xrightarrow{\text{Alkaline Phosphatase}} \text{Gal}$$

In the second reaction, Gal is converted to galactonolactone through the galactose dehydrogenase NAD^+/NADH-coupled reaction.

$$\text{Gal} + \text{NAD}^+ \xrightarrow{\text{Galactose Dehydrogenase}} \text{galactonolactone} + \text{NADH}$$

The NADH produced is proportional to the Gal concentration.

The final reaction, catalyzed by 1-methoxy PMS, employs a tetrazolium salt (MTT) and produces a formazan dye that is measured colorimetrically.

$$\text{NADH} + \text{MTT} \xrightarrow{\text{1-methoxy PMS}} \text{Colored Formazan} + \text{NAD}^+$$

The color developed is proportional to the Total Galactose concentration in the sample. A standard curve prepared from a stock Galactose solution is used to quantitate the results.

Patient samples of whole blood collected on standardized filter paper are placed into the wells of a 96 well filtration microplate. Extraction solution (3% TCA) is added to each well and the samples are eluted at 37 °C for 60 minutes on a plate shaker/incubator. Following incubation the filter plate is placed on a vacuum manifold and its contents filtered into a clean flat-bottom microplate. Enzyme Reagent and Coenzyme Reagent are added to all wells and the plate is incubated at 37 °C for 30 minutes on a plate shaker/incubator. Color Reagent is then added to all wells and the plate is incubated for 10 minutes at 37 °C on a plate incubator/shaker. The absorbance is measured on a microplate reader at a wavelength of 600 nm for the measurement channel and 750 nm for the reference channel. Results are expressed as mg of total galactose per dL of whole blood.

5. Statement of Intended Use

The SPOTCHECK Neonatal Total Galactose Microplate Reagent Kit is intended for the quantitative determination of the concentration of Total Galactose (galactose (Gal) + galactose-1-phosphate (Gal-1-P)) in whole blood saturated filter paper disks using a microplate absorbance reader or SPOTCHECK Pro. Measurements of Total Galactose are used primarily in the diagnosis and treatment of the hereditary disease galactosemia. This method is intended for *in vitro* diagnostic use as an aid in neonatal screening for increased concentrations of Total Galactose, and not for monitoring purposes.

6. Summary of the Technological Characteristics of the Device

DEVICE COMPARISON

The most significant difference between the SPOTCHECK Neonatal Total Galactose Microplate Reagent Kit and the predicate device is the use of liquid calibrants with the proposed device versus dried blood spot calibrants with the predicate. Additionally, the proposed device is also intended for use on automated platforms while the predicate is intended for manual processing only. Both the proposed and predicate devices use

approximately the same reagent formulation and both use the same technology (spectrophotometric microplate reader) to determine total galactose concentration.

Neonatal patient dried blood specimens are punched into microplate wells, eluted and incubated with the same extraction solution on the proposed device as on the predicate device. The Enzyme and Coenzyme reagents are prepared and added as separate reagents on the proposed device, whereas they are combined immediately prior to use on the predicate. The final step in the reaction, the formation of the colored formazan, is the same in both devices.

The predicate device allows a time range for the extraction (45 – 120 minutes) and enzyme incubation (30 – 60 minutes) steps and specifies 5 minutes between color reagent addition and the absorbance measurement. The proposed device specifies the time required for the extraction (60 minutes) and enzyme incubation (30 minutes) steps and calls for 10 minutes between color reagent addition and the absorbance measurement.

Summary of SPOTCHECK Neonatal Total Galactose Microplate Kit and Predicate Device Comparison of Technological Characteristics

Comparator	SPOTCHECK Neonatal Total Galactose Microplate Kit	Predicate Device
Specimen collection, handling and storage	Use standardized blood spot collection cards; follow protocol in *CLSI LA4-A5*	Same collection, handling and storage
Specimen	1 x 1/8" dried blood spot (DBS) disks	Same sample size, has second protocol using 2 x 1/8" disks
Extraction and incubation	In microplate, on combination incubator/shaker	In microplate, on shaker
Extraction and incubation temperature	37 °C	18-25 °C
Extraction time	60 minutes	45 – 120 minutes
Incubation time	30 minutes	30 – 60 minutes
Extraction Solution	3% TCA	3% TCA
Enzyme Reagent	Buffered Alkaline Phosphatase and Galactose Dehydrogenase	Buffered Alkaline Phosphatase, Galactose Dehydrogenase and Nicotinamide adenine dinucleotide (NAD)
Coenzyme reagent	NAD	N/A (NAD included in enzyme reagent, see above)
Color reagent	Buffered MTT + Methoxy PMS	Buffered MTT + Methoxy PMS
Absorbance measurement	600 nm (750 nm reference)	570 nm (690 nm reference)
Reporting units	mg/dL	mg/dL
Limit of quantitation	1.4 mg/dL	1.5 mg/dL
Range	1.4 – 50 mg/dL	1.5 mg/dL – 50 mg/dL

Comparator	SPOTCHECK Neonatal Total Galactose Microplate Kit	Predicate Device
Calibration	Liquid galactose standards	Dried blood spot standards
Clinical classification	Presumptive positive and negative (normal)	Presumptive positive and negative (normal)
Quality control material	Not provided with kit	DBS low, mid, and high concentrations

LINEARITY

The assay is linear in the range of 1.4 to 50 mg/dL, as confirmed by adherence to CLSI EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. Responses of the standards give a correlation coefficient $R^2 > 0.995$ using a 1st order curve from 0 to 50 mg/dL. Total galactose results <1.4 mg/dL and >50 mg/dL are to be reported as such.

ANALYTICAL SENSITIVITY

The analytical sensitivity of the assay was determined by adherence to NCCLS EP17-A *Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline*. The limit of detection (LoD) for Total Galactose utilizing manual processing is 1.4 mg/dL and utilizing SPOTCHECK PRO processing is 1.3 mg/dL, as calculated using the guidelines in NCCLS EP17-A protocol and with proportions of false positives (α) less than 0.1% and false negatives (β) less than 0.1%, based on 180 determinations. For ease of use when utilizing both processing options, the LoQ for SPOTCHECK Pro processing will be set at 1.4 mg/dL. The limit of blank (LoB) utilizing manual processing is 1.1 mg/dL and utilizing SPOTCHECK PRO processing is 0.9 mg/dL. To establish the LoQ, since an estimate of bias is not assured, the following goal for Total Error (TE) was used: "imprecision at any concentration greater than or equal to the LoQ shall not exceed 20%". To evaluate imprecision within the data collected for this study (Sensitivity), %RSD was used as the metric. For both manual and SPOTCHECK PRO processing, %RSD is less than 20 for all levels that are at or above the LoQ.

METHOD COMPARISON

Expected Values, Clinical Cutoff and Sample Classification Comparison

An exemplary normal range was established by analyzing 2037 (2036 for SPOTCHECK Pro) routine samples at a state screening laboratory using the SPOTCHECK Kit both manually and automated. The same specimens were analyzed using a legally-marketed predicate device. In addition, 51 manufactured samples elevated in Total Galactose were tested with both the proposed and predicate devices for the purpose of sample classification comparison.

To supplement the initial clinical comparison study 11 retrospective confirmed galactosemic newborn specimens were obtained from the Michigan Neonatal Biobank. The specimens were blindly added amidst presumptive negative patient specimens and data was collected in two runs on each device over the course of two days in the Quality Control laboratory at Astoria-Pacific, Inc. The supplemental study brought the total

number of neonatal specimens analyzed from 2037 to 2209 (2036 to 2208 for SPOTCHECK Pro). Tables of comparison for sample statistics and a summary of sample classification are provided below.

Data Summary

Total Galactose (mg/dL)	Predicate Device	Proposed Device – Manual	Proposed Device – SPOTCHECK Pro
# of Observations	2268	2268	2267
Mean Value Observed[i]	3.3	3.4	3.6
Standard Deviation[i]	4.7	5.2	5.3
Range of the Data[i]	1.5 – 48.0	1.4 – 49.6	1.4 – 43.1
99th Percentile[ii]	7.2	6.7	7.0
99.5th Percentile[ii]	8.8	8.5	8.9

[i]Results for these statistics only apply to those samples with results ≥LoQ (≥1.4 for Proposed and ≥1.5 for Predicate) and ≤ high calibrant (50 mg/dL for Proposed and Predicate)
[ii]Cutoffs are based on routine neonatal specimens only

Specimens with results greater than the 99 and 99.5 percentiles were classified as presumptive positive for galactosemia, and require follow-up testing according to institutional, local, state, regional, and/or national guidelines or regulations. The same criteria were used for both the proposed device and predicate device. Classification results between the predicate and the SPOTCHECK reagent kits, whether processed manually or using the SPOTCHECK Pro, were substantially equivalent.

PRECISION PERFORMANCE

Within-run and total precision for the proposed device were determined according to CLSI EP5-A2: *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline — Second Edition*. Evaluation of precision utilized samples that were prepared from whole blood, with hematocrit adjusted to 55%, and spiked with analyte at three different concentrations (identified as "normal", "near cutoff" and "galactosemic"). Samples were analyzed over five days, one run per day, sixteen replicates of each sample per run. Within each run two calibration curves were used, each curve was used to quantify half of the replicates for each sample. This was done to capture variation in calibration as a potential source of imprecision. Within-run and total precision using the *predicate device* was determined by analyzing samples in duplicate during 20 separate runs (data reported for the predicate was copied from product insert).

Precision Tables

TGal - Manual	Normal	Near Cutoff	Galactosemic
n (# of observations)	80	80	80
Mean (mg/dL)	3.5	10.0	31.3
S_r (within-run precision)	0.291	0.640	1.401
C.V. (within-run)	8.3	6.4	4.5
B (daily mean precision)	0.194	0.453	0.661
S_T (total precision)	0.342	0.768	1.509
C.V. (total)	9.8	7.7	4.8

Precision Tables (continued)

TGal - SPOTCHECK Pro	Normal	Near Cutoff	Galactosemic
n (# of observations)	80	80	80
Mean (mg/dL)	3.3	10.2	33.1
S_r (within-run precision)	0.249	0.593	1.465
C.V. (within-run)	7.5	5.8	4.4
B (daily mean precision)	0.122	0.324	0.937
S_T (total precision)	0.270	0.659	1.700
C.V. (total)	8.2	6.5	5.1

TGal – Predicate (manual)	CDC 721	CDC 722	CDC 723	CDC 724
n (# of observations)	40	40	40	40
Mean (mg/dL)	6.1	10.4	14.9	29.4
S_r (within-run precision)	0.5	0.7	0.7	1.7
C.V. (within-run)	8.2	6.7	4.7	5.8
B (daily mean precision)	0.5	0.6	1.0	2.1
S_T (total precision)	0.6	0.8	1.1	2.4
C.V. (total)	9.6	7.8	7.5	8.0

The results of the precision study demonstrate that the SPOTCHECK Neonatal Total Galactose Microplate Reagent Kit, at a minimum, exhibits comparable precision performance to that reported in the predicate device insert. Additionally, performance is similar whether the SPOTCHECK kit is processed manually or with automation.

ANALYTICAL SPECIFICITY

The study of potential interfering substances when using the SPOTCHECK Neonatal Total Galactose Microplate Reagent Kit was carried out according to CLSI EP7-A2: *Interference Testing in Clinical Chemistry; Approved Guideline — Second Edition.*

Interference Evaluated	SPOTCHECK Neonatal Total Galactose Microplate Kit	Predicate Device Claims
γ globulin (protein)	Up to 6000 mg/dL showed no statistically significant interference	Up to 6000 mg/dL showed no significant interference
Albumin (protein)	Up to 6000 mg/dL showed no statistically significant interference	Up to 10000 mg/dL showed no significant interference
Bilirubin, conjugated	Up to 20 mg/dL showed no statistically or clinically significant interference	Up to 20 mg/dL showed no significant interference
Bilirubin, unconjugated	Up to 20 mg/dL showed no statistically or clinically significant interference	Up to 20 mg/dL showed no significant interference
Hemoglobin (Hb)	Up to 200 mg/dL showed no statistically or clinically significant increase	Up to 20000 mg/dL showed no significant interference

Interference Evaluated	SPOTCHECK Neonatal Total Galactose Microplate Kit	Predicate Device Claims
Lipid	Up to 3264 mg/dL showed statistically significant interference at low (normal) concentrations; the result is not clinically significant	Up to 2700 mg/dL showed no significant interference
Sulfamethoxazole (SMX)	Up to 4 mg/dL showed no statistically or clinically significant interference	Not evaluated
Trimethoprim (TMP)	Up to 4 mg/dL showed statistically significant interference at low (normal) concentrations; the result is not clinically significant	Not evaluated
Fructose	Up to 25 mg/dL showed statistically significant interference at low (normal) concentrations; the result is not clinically significant	Up to 25 mg/dL showed no statistically or clinically significant interference
Glucose	Up to 1200 mg/dL showed no statistically or clinically significant interference	Up to 1200 mg/dL showed no statistically or clinically significant interference
Ascorbate	Up to 6 mg/dL showed no statistically or clinically significant interference	Up to 3 mg/dL showed no statistically or clinically significant interference
Mannose	Up to 5 mg/dL showed no statistically or clinically significant interference	Up to 5 mg/dL showed no statistically or clinically significant interference
Glutathione	Up to 60 mg/dL showed statistically significant interference at low (normal) concentrations and increased response at all concentrations, which could result in a false positive	Up to 60 mg/dL showed no statistically or clinically significant interference

7. Determination of Substantial Equivalency

Based on the performance characteristics and comparison data, the proposed device is safe, effective, and substantially equivalent to the legally-marketed predicate device. The indications for use are fundamentally the same for the SPOTCHECK Neonatal Total Galactose Microplate Reagent Kit and the predicate device. Technological and performance characteristics are very similar to the predicate device and there is sufficient evidence that demonstrates that the differences do not adversely affect the safety and effectiveness of the proposed device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

June 20, 2013

Astoria-Pacifica, Inc.
C/O Charles Peterson
President
15130 S.E. 82nd Drive
P.O. Box 830
CLACKAMAS OR 97015-0830

Re: K121101
Trade/Device Name: SPOTCHECK Neonatal Total Galactose Microplate Reagent Kit
Regulation Number: 21 CFR 862.1310
Regulation Name: Galactose test system
Regulatory Class: I, exceeds the limitation to exemption in 862.9(c)(2)
Product Code: JIA
Dated: June 7, 2013
Received: June 11, 2013

Dear Mr. Peterson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director, Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use Form

510(k) Number (if known): k121101

Device Name: SPOTCHECK® Neonatal Total Galactose Microplate Reagent Kit

Indications for Use:

The SPOTCHECK® Neonatal Total Galactose Microplate Reagent Kit is for the quantitative determination of the concentration of Total Galactose (galactose (Gal) + galactose-1-phosphate (Gal-1-P)) in whole blood saturated filter paper disks, using a microplate absorbance reader or SPOTCHECK Pro. Measurements of Total Galactose are used primarily in the diagnosis and treatment of the hereditary disease galactosemia. This method is intended for in vitro diagnostic use as an aid in neonatal screening for increased concentrations of Total Galactose, and not for monitoring purposes.

Prescription-Use X AND/OR Over-The-Counter-Use
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Yung W. Chan -S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k) k121101